CLAIMS

1. A single chain polypeptide comprising first and second domains, wherein:-
said first domain is a clostridial neurotoxin light chain or a fragment or a variant thereof, wherein said first domain is capable of cleaving one or more vesicle or plasma membrane associated proteins essential to exocytosis; and
said second domain is a clostridial neurotoxin heavy chain H_N portion or a fragment or a variant thereof, wherein said second domain is capable of (i) translocating the polypeptide into a cell or (ii) increasing the solubility of the polypeptide compared to the solubility of the first domain on its own or (iii) both translocating the polypeptide into a cell and increasing the solubility of the polypeptide compared to the solubility of the first domain on its own; and said second domain lacks a functional C-terminal part of a clostridial neurotoxin heavy chain designated H_C thereby rendering the polypeptide incapable of binding to cell surface receptors that are the natural cell surface receptors to which native clostridial neurotoxin binds; and wherein said single chain polypeptide comprises a sequence selected from the group consisting of:-

(I) SEQ ID NO: 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 139, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, and 175; or

(II) a fragment or variant of (I) having a first domain that is capable of cleaving one or more vesicle or plasma membrane associated proteins essential to exocytosis.

2. A polypeptide according to Claim 1 wherein said clostridial toxin heavy chain is a botulinum neurotoxin heavy chain.

3. A polypeptide according to Claim 1 wherein said clostridial toxin heavy chain is a tetanus neurotoxin heavy chain.

4. A polypeptide according to any preceding claim, wherein the first domain exhibits endopeptidase activity specific for a substrate selected from one or more of SNAP-25, synaptobrevin/VAMP and syntaxin.

5. A polypeptide according to any preceding claim, wherein said second domain is a clostridial toxin heavy chain H_N portion.

6. A polypeptide according to Claim 1, wherein said clostridial neurotoxin heavy chain is a botulinum neurotoxin type A chain.

7. A polypeptide according to Claim 1, wherein the second domain comprises the 423 N-terminal amino acids of botulinum toxin type A heavy chain.

8. A polypeptide according to Claim 1, wherein said clostridial neurotoxin heavy chain is a botulinum neurotoxin type B chain.

9. A polypeptide according to Claim 1, wherein the second domain comprises the 107 N-terminal amino acids of a botulinum toxin type B heavy chain.

10. A polypeptide according to Claim 1, wherein the second domain comprises the 417 N-terminal amino acids of botulinum toxin type B heavy chain.

11. A polypeptide according to Claim 1 wherein the second domain comprises the 422 N-terminal amino acids of tetanus heavy chain.

12. A polypeptide according to Claim 1 wherein the second domain comprises the 100 N-terminal amino acids of a clostridial neurotoxin heavy chain.

13. A polypeptide according to Claim 1 comprising a site for cleavage by a proteolytic enzyme.

14. A polypeptide according to Claim 13, wherein the cleavage site is not present in

a native clostridial neurotoxin.

15. A polypeptide according to Claim 13 or Claim 14, wherein the cleavage site allows proteolytic cleavage of the first and second domains.

16. A polypeptide according to any of Claims 13-15, wherein the cleavage site allows proteolytic cleavage of the first and second domains, and when so cleaved said first domain exhibits greater enzyme activity in cleaving said one or more vesicle or plasma membrane associated protein than does the polypeptide prior to said proteolytic cleavage.

17. A polypeptide according to any of Claims 13-16 obtainable by providing a first nucleic acid sequence encoding said cleavage site within a second nucleic acid sequence encoding a peptide according to Claim 1.

18. A polypeptide according to any preceding claim, wherein the second domain lacks a C-terminal part of a clostridial neurotoxin heavy chain designated H_C.

19. A polypeptide according to any preceding claim, further comprising a third domain that binds the polypeptide to a cell, by binding of the third domain directly to a cell or by binding of the third domain to a ligand or to ligands that bind to a cell.

20. A polypeptide according to Claim 19, wherein said third domain is for binding the polypeptide to an immunoglobulin.

21. A polypeptide according to Claim 20, wherein said third domain is a tandem repeat synthetic IgG binding domain derived from domain b of Staphylococcal protein A.

22. A polypeptide according to Claim 19, wherein said third domain comprises an amino acid sequence that binds to a cell surface receptor.

23. A polypeptide according to Claim 22, wherein said third domain is insulin-like

growth factor-1 (IGF-1).

24. A polypeptide according to any preceding claim including a spacer molecule between the first and second domains.

25. A polypeptide according to any of Claims 19-23 including a spacer molecule between the second and third domains.

26. A polypeptide according to any preceding claim, further comprising a purification tag that binds to an affinity matrix thereby facilitating purification of the polypeptide using said matrix.

27. A polypeptide according to Claim 26 including a spacer molecule between the purification tag and the polypeptide.

28. A polypeptide according to Claim 26 or Claim 27, wherein said purification tag binds to an affinity matrix of glutathione sepharose.

29. A polypeptide according to any of Claims 26-28, wherein a first protease cleavage site is incorporated between the polypeptide according to any of Claim 1-23 and the purification tag, said protease cleavage site enabling proteolytic separation of said polypeptide from said purification tag.

30. A polypeptide according to any of Claims 26-29, wherein a second proteolytic cleavage site is incorporated between the first and second domains of the polypeptide according to any of Claims 1-23, said protease cleavage site enabling proteolytic cleavage of the first and second domains.

31. A nucleic acid encoding a polypeptide according to any preceding claim.

32. A nucleic acid according to Claim 31, wherein said nucleic acid lacks nucleotides encoding a portion designated H_C of a clostridial neurotoxin.

33. A nucleic acid according to Claim 31 or Claim 32, comprising nucleotides encoding residues 1-423 of a botulinum toxin type A heavy chain H_N domain.

34. A nucleic acid according to Claim 31 or Claim 32, comprising nucleotides encoding residues 1-417 of a botulinum toxin type B heavy chain H_N domain.

35. A nucleic acid according to any of Claims 31-34, comprising nucleotides encoding a proteolytic cleavage site.

36. A nucleic acid according to Claim 35, wherein the proteolytic cleavage site is not present in a native clostridial neurotoxin.

37. A nucleic acid according to Claim 36, wherein said proteolytic cleavage site is located between the first and second domains of the polypeptide.

38. A nucleic acid according to Claim 36 or 37, obtainable by providing a nucleic acid sequence encoding said cleavage site within a nucleic acid sequence according to Claim 29.

39. A nucleic acid sequence selected from the group consisting of:- SEQ ID 69, 71, 73, 75, 77, 113, 134, or a fragment or variant thereof.

40. A single chain polypeptide selected from the group consisting of:- SEQ ID 70, 72, 74, 76, 78, 114, or a fragment or variant thereof.